

### REMARKS

Reconsideration of the present application in light of the above amendments and the following remarks is respectfully requested. Claims 8-9 and 17-24 have been canceled. Claims 1-7 and 10-16 are pending. Claims 1 and 7 have been amended for clarification. Support for the amendments may be found, for example, at lines 6-10, page 5; lines 24-28, page 17; and lines 8-11, page 18, lines. Applicant notes the inadvertent deletion of the word “and” prior to “a substrate” in the Amendment dated November 3, 2005, which is corrected by the current amendment to claim 1. No new matter has been added to the application by way of amendment.

### Objection to the Priority Claim

Applicant thanks the Examiner for granting priority for all pending claims (claims 1-7 and 10-16) of the present application under 35 U.S.C. § 119(e) to Provisional Application No. 60/228,956, filed August 28, 2000, as well as for granting priority for claims 1-6 and 10-16 under 35 U.S.C. § 120 to parent U.S. Application No. 09/484,593, now U.S. Patent No. 6,387,650.

Applicant traverses the denial of claim 7 of the priority claim to U.S. Application No. 09/484,593, now U.S. Patent No. 6,387,650 (“the parent application”). Specifically, the Action alleges the parent application does not disclose a conditionally detectable marker to be detectable by a change in color, produced by the biochemical reduction of tetrazolium red, but concedes that the parent application teaches a signal moiety linked to the substrate, wherein the signal moiety can be cleaved to produce a detectable signal.

Applicant respectfully disagrees with the Action’s characterization of certain subject matter contained in the present and parent applications. In particular, Applicant notes that in the present application, “conditionally detectable marker” is defined as any molecule that undergoes a measurable change (such as color change) when reacted upon by a viable microorganism in a sample. (See lines 25-27, pg. 8 of the instant specification.)

Further, Applicant notes that the parent application discloses measuring bacterial concentration in food by measuring specific metabolic by-products of individual microorganisms. Some methods of measurement that include color changes associated with microbe growth are disclosed as phenol red, bromocresol blue, neutral red, dioxanes, tropinones,

and tetrazolium. (See lines 39-61, Col. 1, U.S. Patent No. 6,387,650.) More specifically, the parent application incorporates by reference U.S. Patent No. 4,129,483, which describes using a nonbiodegradable substance (tetrazolium) that is chemically reduced to produce a color change. (See lines 57-59, Col. 1, U.S. Patent No. 6,387,650.) Thus, the subject matter relating to using tetrazolium red as one form of a “conditionally detectable marker,” as claimed in claim 7, is explicitly disclosed in the present application.

Accordingly, Applicant respectfully submits that the priority claim to the parent application is proper for claim 7, for reasons that parallel the basis for priority granted to the other presently pending claims. Applicant respectfully requests priority to the parent application be granted to claim 7 as well.

**Claim Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-7 and 10-16 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Action alleges claim 1 is unclear as to the terms “substrate,” “conditionally detectable marker,” and “substantially;” and claim 1 is allegedly unclear as to whether the composition functions to detect target microorganisms or non-target microorganisms. The Action further alleges it is unclear whether tetrazolium red is a conditional marker in claim 7.

Applicant traverses this rejection and respectfully submits that the present claims particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant submits that the Action misinterprets the essence of the present application. As discussed in the instant specification, the present application discloses a composition incorporating a detection scheme in the growth medium comprising both presumptive positive and confirmed positive indicators for a target microorganism. (See lines 22-23, pg. 19, of the instant specification.) Briefly, the presumptive indicator (which is represented by the conditionally detectable marker in present claim 1) is reacted by both viable target microorganisms and any viable non-target microorganisms in the medium, and results in the production of a measurable signal (indicated by color change, for example, by the reduction of tetrazolium red).

The confirmed indicator (which is represented by the substrate comprising a signal moiety in present claim 1) is reacted upon substantially only by the non-target microorganisms, and results in a detectable signal (such as by the hydrolysis of the substrate). (See lines 24-28, pg. 19 and lines 9-12, pg. 20 of the instant specification.) Thus, the combination of both the conditionally detectable marker (presumptive indicator) and the *absence* of a signal from the substrate--signal moiety (confirmed indicator) detect the presence of the target microorganism. (See lines 27-30, pg. 19 of the instant specification.) Applicant respectfully asserts that, contrary to the Action's characterization, the presently claimed compositions indeed detect the presence of the *target* microorganism, as set forth in the preamble of claim 1.

Regarding the clarity of specific terms used in claim 1, including "substrate," "conditionally detectable marker," and "substantially," Applicant respectfully submits these terms are clearly defined in the instant specification. For example, the definition for "enzyme substrate" may be found, among others, at lines 11-20, page 9 of the instant specification; the definition for "conditionally detectable marker" may be found, among others, at line 25, page 8—line 10, page 9 of the instant specification; and the term "substantially" is defined, among others, at lines 26-28, page 11 of the instant specification. Applicant respectfully asserts that one of skill in the art would fully appreciate the use of these terms in the context of the claims, when read in light of the definitions provided in the instant specification. Nonetheless, solely to expedite prosecution and without acquiescing to any rejection, Applicant submits claim 1 has been amended for clarification.

With regard to claim 7, Applicant submits the claim distinctly sets forth the subject matter of the present application. Nonetheless, solely to expedite prosecution and without acquiescing to this rejection, Applicant submits claim 7 has been amended for clarification. Support for the amendments may be found, for example, at lines 6-10, page 5; lines 24-28, page 17; and lines 8-11, page 18. Accordingly, Applicant submits the grounds for this rejection have been obviated and respectfully requests this rejection be withdrawn.

**Claim Rejections Under 35 U.S.C. § 102, First Rejection**

Claims 1-6 and 10-16 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Carr et al. (U.S. Patent 5,064,756). The Action alleges Carr et al. anticipate the presently claimed invention by teaching a kit for antibiotic sensitivity testing comprising a prepared microtiter plate containing active materials, antibiotics, and one or more fluorogens.

Applicant respectfully traverses this rejection and submits the cited reference does not anticipate the presently claimed invention. Specifically, Applicant notes Carr et al. teach methods for detection of a target microbe by the ability of the *target microbe* to hydrolyze a specifically chosen substrate. Applicant respectfully submits this is directly contrary to the presently claimed compositions for detecting a target microorganism comprising a substrate for an aminopeptidase, wherein said aminopeptidase is substantially *absent* from the target microorganism, wherein said substrate comprises a signal moiety, the signal moiety capable of providing a detectable signal when cleaved by substantially all *non-target microorganisms*.

In addition, Applicant submits Carr et al. fail to teach methods for employing a conditionally detectable marker in addition to a substrate for an aminopeptidase, as claimed in the compositions of the present application. Thus, Carr et al. fail to teach each and every element of the presently claimed compositions. Indeed, Carr et al. fail to teach *any* element of the presently claimed compositions. Accordingly, Applicant respectfully submits the grounds for this rejection have been overcome and requests this rejection be withdrawn.

**Claim Rejections Under 35 U.S.C. § 102, Second Rejection**

Claims 1-6 and 10-13 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Manafi, et al (*J. Applied Bacteriology*, 1990). The Action alleges Manafi et al. anticipates the presently claimed invention by teaching a composition comprising L-alanine-7-amido-4-methylcoumarin (AAMC), which produces a fluorescent color change when cleaved by the L-alanine-aminopeptidase found in the cell wall of Gram-negative bacteria.

Applicant respectfully traverses this rejection and submits the cited reference does not teach each and every element of the presently claimed compositions. Specifically, Applicant

notes the cited reference discloses a method that provides a secondary confirmation for Gram staining. However, Applicant respectfully asserts that the cited reference fails to contemplate the presently claimed compositions comprising a conditionally detectable marker and a substrate for an aminopeptidase, wherein said aminopeptidase is substantially absent from the target microorganism, wherein said substrate comprises a signal moiety, the signal moiety capable of providing a detectable signal when cleaved by substantially all non-target microorganisms. While the cited reference discloses a laundry list of bacterial enzyme substrates, it nowhere considers compositions for detecting a target microorganism comprising the combination of both a conditionally detectable marker and a substrate for an aminopeptidase, wherein said aminopeptidase is substantially *absent* from the target microorganism. Accordingly, Applicant respectfully submits the grounds for this rejection have been overcome and requests the rejection be withdrawn.

#### **Claim Rejections Under 35 U.S.C. § 102, Third Rejection**

Claims 1-7 and 13 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Tuompo et al. (U.S. Patent No. 5,420,017). The Action alleges Tuompo et al. teach a composition for detecting Gram-negative bacteria, wherein the composition comprises a test solution of a chromogenic reagent used to detect Gram-negative bacteria, and wherein in certain aspects the chromogenic reagent is tetrazolium red.

Applicant respectfully traverses this rejection and submits the cited reference does not anticipate the presently claimed invention. Applicant submits that the cited reference merely claims methods and test kits for detecting Gram-negative bacteria that include multiple steps, including filtering a solution, washing the filter, and examining the filter for the presence of a color change, which indicates the presence of Gram-negative bacteria. The cited reference does not contemplate the presently claimed compositions relating to detecting a target microorganism comprising the combination of both a conditionally detectable marker and a substrate for an aminopeptidase, wherein the aminopeptidase is substantially *absent* from the target microorganism. Thus, the cited reference does not teach each and every element of the presently claimed compositions. Accordingly, Applicant respectfully submits the grounds for this rejection have been overcome and requests the rejection be withdrawn.

**Claim Rejections Under 35 U.S.C. § 103, First Rejection**

Claims 1-6 and 10-13 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Carr et al. (U.S. Patent No. 5,064,756). Specifically, the Action alleges that it would have been obvious to one of skill in the art to use any well-known amino acid-containing derivative for use in detecting bacteria upon reading Carr et al.

Applicant respectfully traverses this rejection and submits the Action fails to establish a *prima facie* case of obviousness since the Action fails to establish any suggestion or motivation in the cited reference that would lead one of ordinary skill in the art to arrive at the presently claimed compositions. Applicant respectfully submits that no such suggestion or motivation exists in the cited reference because the cited reference actually teaches away from the presently claimed compositions. Applicant reiterates that Carr et al. claim methods of detecting a target microbe based on the ability of the target microbe to hydrolyze specific substrates. Applicant respectfully asserts that the presently claimed compositions comprise a substrate for an aminopeptidase, wherein said aminopeptidase is substantially *absent* from the target microorganism. Applicant submits that one of skill in the art, upon review of the cited reference, would not expect to detect a target microorganism based on the *absence* of hydrolysis of the chosen substrate.

Applicant further submits that the cited reference nowhere considers methods employing the combination of both a conditionally detectable marker and a substrate for an aminopeptidase, wherein said aminopeptidase is substantially absent from the target microorganism, for detecting the target microorganism. Accordingly, Applicant respectfully submits the grounds for this rejection have been overcome, and requests the rejection be withdrawn.

**Claim Rejections Under 35 U.S.C. § 103, Second Rejection**

Claims 1-6 and 10-13 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Manafi et al. (*J. Applied Bacteriology*, 1990). In particular, the Action alleges that the cited reference teaches methods of detecting Gram-negative bacteria using L-alanine-7-amido-4-methylcoumarin as a substrate, and further alleges that it would be within the purview

of one of ordinary skill in the art to utilize any functional equivalent substrate to do the same to arrive at the presently claimed compositions.

Applicant respectfully traverses this rejection and submits that the Action has failed to establish a *prima facie* case of obviousness with regard to Manafi et al., since the Action fails to point out any suggestion or motivation in the cited reference for one of ordinary skill in the art to be led to the presently claimed compositions. Applicant respectfully submits the cited reference provides no such suggestion or motivation because the reference provides for methods of using possible substrates for confirming bacterial Gram-staining, but in no way considers the presently claimed compositions. Applicant asserts one of ordinary skill in the art, upon review of the cited reference, would not be motivated to arrive at the presently claimed compositions for detecting a target microorganism wherein said compositions comprise both a conditionally detectable marker as well as a substrate for an aminopeptidase, wherein said aminopeptidase is substantially absent from the target microorganism. Thus, the cited reference fails to suggest or motivate one of ordinary skill in the art to arrive at the presently claimed compositions. Accordingly, Applicant respectfully submits the grounds for this rejection have been overcome and request the rejection be withdrawn.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

A handwritten signature in black ink, appearing to read "Melanie K. Kitzan Haindfield", is written over a horizontal line.

Melanie K. Kitzan Haindfield, Ph.D.  
Registration No. 57,397

MKH:

Enclosure:  
Postcard

701 Fifth Avenue, Suite 6300  
Seattle, Washington 98104-7092  
Phone: (206) 622-4900  
Fax: (206) 682-6031

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